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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/667,271	09/16/2003	James McSwiggen	MBHB02-763-B(400/129))	8658

20306 7590 04/18/2007
MCDONNELL BOEHNEN HULBERT & BERGHOFF LLP
300 S. WACKER DRIVE
32ND FLOOR
CHICAGO, IL 60606

EXAMINER

BOWMAN, AMY HUDSON

ART UNIT	PAPER NUMBER
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1635

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

10/667,271

Applicant(s)

MCSWIGGEN ET AL.

Examiner

Amy H. Bowman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 February 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,15-18,20,32 and 36-39 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,15-18,20,32 and 36-39 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 16 September 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date. _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of Application/Amendment/Claims

Applicant's response filed 2/28/07 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 8/28/06 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 15-18, 20, 32, and 36-39 are pending in the application.

Applicant's amendments and/or arguments filed on 2/28/07, with respect to the claim objections have been fully considered and are persuasive. Therefore, the objections/rejections have been withdrawn. However, the rejections addressed below are pending.

Response to Priority

The effective filing date of the instant claims is determined to be that of PCT/US03/05043, which has an effective filing date of 2/20/2003. The earlier documents do not teach every limitation of the instant claims,

Applicant points to support in application 60/363,124 for some of the instant limitations. However, the claims are essential subject matter. Essential subject matter may be incorporated by reference, but only by way of incorporation by reference to a

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U.S. patent or U.S. patent application publication, whereas application '124 is a provisional application. See MPEP 608.01(p) and 37 CFR 1.57.

Furthermore, application '124 does not teach every limitation of the instant claims. For example, application '124 does not teach a limitation wherein "about 100 percent of the nucleotide positions in one or both strands of the siRNA molecule are chemically modified" and "the antisense strand of the siRNA molecule comprises about 5, 6, 7, 8, 9, 10 or more 2'-O-methyl nucleotides", as instantly recited in claim 1.

Should applicant disagree, applicants are encouraged to point out with particularity by page and line number where such support might exist for each claim limitation in each of the claimed priority documents.

Response to Claim Rejections - 35 USC § 103

Claims 1, 15-18, 20, 32, and 36-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wu et al. (Croatian Medical Journal, 42(4), 2001, pages 463-466), in view of Elbashir et al. (The EMBO Journal, Vol. 20, No. 23, pages 6877-6888, 2001), Pavco et al. (US 6,346,398 B1), Hammond et al. (Nature, 2001, Vol. 2, pages 110-119), Caplen (Expert Opin Biol Ther, 2003 Jul, 3(4), pp. 575-86), and Parrish et al. (Molecular Cell, Vol. 6, pages 1077-1087, 2000), for the reasons of record set forth in the office action mailed on 2/28/07.

Applicant has cancelled claims 5 and 29, thereby obviating the rejection against these claims.

Applicant argues that none of the references cited by the examiner, alone or in combination, make obvious the presently claimed constructs in which about 100 percent of the nucleotide positions in one or both strands of the siRNA molecule are chemically modified and the antisense strand of the siRNA molecule comprises about 5, 6, 7, 8, 9, 10 or more 2'-O-methyl nucleotides.

Applicant further asserts that none of the art, alone or in combination provides any insight into whether such highly modified double stranded siRNA nucleic acid constructs would function. Contrary to applicant's assertion, Elbashir et al. teach chemically modified siRNA molecules that retain siRNA activity when modified at 19% of the nucleotide positions and Parrish et al. teach extensively modified dsRNA molecules that retained RNAi activity. Applicant asserts that Parrish et al. teach away from highly modified siRNA constructs and points to pages 1081 and 1082, figures 5 and 6 of Parrish et al. Contrary to applicant's assertion, Parrish et al. teach extensively modified dsRNA molecules that retain interference activity.

Applicant further asserts that that Elbashir et al. expressly teaches away from highly modified siRNA constructs based on a passage from "The siRNA User Guide" section of Elbashir et al. It is noted that Elbashir et al. teach that 100% modification of one or both strands with 2'-deoxy or 2'-O-methyl modifications abolished RNAi activity. However, there are not any instantly pending claims that are directed to siRNA molecules with these specific structural characteristics and therefore Elbashir et al. do not teach away from the instant claims.

Applicant asserts that because the only teaching in Elbashir addressing the issue of the degree of modifications tolerated in siRNA molecules expressly states that more than a few end modifications should be avoided, it could not have been obvious to make the highly modified constructs now being claimed. Applicant's interpretation regarding the passage in the Elbashir et al. reference is considered erroneous. Elbashir et al. teach chemical modification of siRNA duplexes with 2'-deoxy or 2'-O-methyl modifications and teach modification of 19% of the nucleotides with 2'-deoxy modifications with successful RNAi activity. Elbashir et al. teach that 100% modification of one or both strands abolished activity. This 100% modification is the modification that is being referred to by Elbashir et al. in the passage cited by applicant referring to "more extensive" modification of siRNAs. Elbashir et al. is silent to any modification percentages between the successful example and the loss of activity at 100% and is silent to any other types of chemical modifications at any percentage.

It is noted that Elbashir et al. teach that 100% modification of one or both strands with 2'-deoxy or 2'-O-methyl modifications abolished activity, as addressed above. However, regardless of the results of these specific modifications at 100% of the positions of one or both strands, Elbashir et al. did modify duplexes and published data regarding successful inhibition with some duplexes and unsuccessful inhibition with others, supporting that testing of such known chemical modifications is routine in the art. The results of Elbashir et al. and Parrish et al. are considered to offer motivation to incorporate chemical modifications at various percentages to optimize the activity of the duplex because not all modifications result in activity at every percentage. Although

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applicant asserts that the office makes no mention of the activity of chemically modified siRNA molecules targeted to HCV, the entire basis of the instant rejection is on enhanced activity of siRNA molecules and the motivation to target one to HCV.

Claims 1, 15-18, 20, 32, and 36-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over McCaffrey et al. (Nature, Vol. 418, July 2002, pages 38-39), in view of Elbashir et al. (The EMBO Journal, Vol. 20, No. 23, pages 6877-6888, 2001), Pavco et al. (US 6,346,398 B1), Caplen (Expert Opin Biol Ther, 2003 Jul, 3(4), pp. 575-86), and Parrish et al. (Molecular Cell, Vol. 6, pages 1077-1087, 2000), for the reasons of record set forth in the office action mailed on 2/28/07.

Applicant has cancelled claims 5 and 29, thereby obviating the rejection against these claims.

Although applicant asserts that the office makes no mention of the activity of chemically modified siRNA molecules targeted to HCV, the entire basis of the instant rejection is on enhanced activity of siRNA molecules and the motivation to target one to HCV. Applicant does not provide any further arguments that are not addressed in the rejection under 35 U.S.C. 103(a) above. Since McCaffrey et al. teach siRNA molecules directed to HCV and the chemical modifications were known in the art to benefit dsRNA molecules, including siRNA molecules, one would certainly expect for the modifications to add the same benefits to the siRNA molecules of McCaffrey et al.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy H. Bowman whose telephone number is (571) 272-0755.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Amy H Bowman
Examiner
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AHB



JON E. ANGELL, PH.D.
PRIMARY EXAMINER